REMARKS

Claims 5, 6, 9-12, and 14-16 are pending in the present application.

The rejection of Claims 5, 6, 9-12, 15, and 16 under 35 U.S.C. §112, second paragraph, is obviated by amendment.

This ground of rejection is based on the Examiner's allegation that the claims lack a nexus between the labeled antibody and the protein targeted by the drug. To address this criticism, Claim 5 has been amended to define the screening step as: contacting a sample containing the proteins obtained from the cDNA expression library with the probe to form a complex between the probe and proteins having a binding affinity for the drug contained in the probe, contacting the complex with a labeled antibody specific for the antigenic substance in the probe, washing the sample to remove any non-bound antibody, and detecting the presence of the labeled antibody which has bound to the antigenic substance.

In view of the foregoing amendment, Applicants request withdrawal of this ground of rejection.

The rejections of (a) Claims 5, 6, 9-10, and 15 under 35 U.S.C. §103(a) over Gram et al in view of Odink et al, Pecht et al, and the Examiner's interpretation of the specification at page 3, lines 19-22, and (b) Claims 11-12 and 16 under 35 U.S.C. §103(a) over Gram et al in view of Odink et al, Pecht et al, the Examiner's interpretation of the specification at page 3, lines 19-22, and Barbas et al, are respectfully traversed.

The present invention provides a method for *in vitro* detection of a gene encoding a drug-targeted protein, comprising

linking an antigenic substance to a drug via a chemical cross-linker to form a probe, wherein the drug is non-protein and *per se* exhibits no antigenicity and wherein the antigenic substance is serum albumin or fluorescein isothiocyanate and wherein the chemical cross-linker is selected from the group consisting of glutaraldehyde, hexamethylene diisocyanate, hexamethylene diisothiocyanate, N,N'-poly(methylene)bis(iodoacetamide), N,N'-ethylenebis(maleimide), ethylene glycol bis(succinimidyl) succinate, sulfosuccinimidyl-4-(p-maleimidophenyl) buryrate, and bisdiazobenzidine;

screening for the gene encoding a protein targeted by said drug, wherein said protein is expressed from a cDNA expression library from a human cell, by using an antigen-antibody reaction between the antigenic substance of the probe and a labeled antibody specific for the antigenic substance, wherein said screening comprises contacting a sample containing the proteins obtained from the cDNA expression library with the probe to form a complex between the probe and proteins having a binding affinity for the drug contained in the probe, contacting the complex with a labeled antibody specific for the antigenic substance in the probe, washing the sample to remove any non-bound antibody, and detecting the presence of the labeled antibody which has bound to the antigenic substance; and

determining the gene sequence of the protein expressed from the cDNA expression library within the probe-bound is contained in a phage vector (see Claim 5).

Applicants note that, for the following reasons, the art of record cannot affect the patentability of the presently pending claims.

Gram et al disclose a method for *in vitro* detection of monoclonal antibodies from a combinatorial library that bind to a progesterone-bovine serine albumin conjugate. However, Applicants note that the disclosure by Gram et al is limited to cDNA libraries of *mouse* origin (see page 3577, left column, under "RNA Isolation and cDNA Synthesis"), whereas the present invention is limited to a cDNA source of *humans*. MPEP §2142 states: "To establish

a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation... to modify the reference... Second, there must be a reasonable expectation of success. Finally, the prior art reference... must teach or suggest all the claim limitations." At no point do Gram et al disclose or suggest using human cDNA. Further, Pecht et al, the specification at page 3, lines 19-22, and Barbas et al also fail to disclose or suggest such a modification. Therefore, the first and third criteria of MPEP §2142 are not satisfied and, as such, no *prima facie* case of obviousness can be found.

In the outstanding Office Action, the Examiner has indicated that the previous rejections over only the foregoing combination of disclosures (i.e., Gram et al, Pecht et al, and the specification at page 3, lines 19-22, with or without Barbas et al) have been withdrawn in view of the amendment in the response filed on February 9, 2005, to define the cDNA expression library as being obtained from a human cell. Nonetheless, the Examiner has substantially repeated the previous rejection, but has merely added Odink et al to the previous collection of references. The Examiner points to Odink et al and alleges that this disclosure cures the aforementioned deficiency in the disclosures of Gram et al and Pecht et al. Specifically, the Examiner cites Odink et al as providing basis for the making cDNA expression library from human cells.

Applicants remind the Examiner "The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990)" (MPEP §2143.01). Therefore, absent some specific disclosure in Odink et al, Gram et al, or Pecht et al to direct the artisan to combine Odink et al with the other references, this rejection must fail.

Applicants submit that the rejection is flawed and cannot stand because (in addition to the foregoing) there would be no motivation to combine the disclosures of Gram et al and

Pecht et al. Specifically, Applicants note that Gram et al and Pecht et al are nonanalogous art (i.e., different fields of endeavor) as are the present invention and the disclosure of Pecht et al. As the examiner notes, Gram et al disclose a method for *in vitro* detection of monoclonal antibodies from a combinatorial library that bind to a progesterone-bovine serine albumin conjugate (e.g., phage display), which requires intact cells. In contrast, Pecht et al disclose bifunctional reporters for immunoprecipitation methods. As is widely appreciated by anyone possessing a technician's level of training in the art, phage display and immunoprecipitation are completely distinct methods, which operate in virtually opposite manners (*i.e.*, phage display requires intact cell membranes, while immunoprecipitation requires lysed cells in order to operate). Accordingly, in view of the significant divergence in the techniques of Gram et al and Pecht et al, there would be no motivation to combine the disclosures of these references.

Moreover, Applicants submit that there is no motivation to combine Odink et al with either Gram et al or Pecht et al, individually or in combination. In citing Odink et al the Examiner asserts that this reference provides motivation for screening for pharmaceutical compounds. However, the disclosure of Odink et al does not support this assertion. The only disclosure in Odink et al is the unsupported statement at column 13, line 66 to column 14, line 2. Certainly Odink et al do not disclose or suggest the use of human cDNA expression libraries for detection of drug-protein interactions. In fact, it appears that this reference is specifically related the therapeutic efficacy of a 160kDa polypeptide as a mediator of inflammation and to influence inflammatory processes, which certainly has no broad application as alleged by the Examiner much less a suggestion to support combination with the disclosures of Gram et al and Pecht et al as required by MPEP §2143.01.

Moreover, as conceded by the Examiner, Gram et al is silent with respect to the specific cross-linking agents in previously Claim 5 from which the remaining claims depend.

Where Gram et al is cited for disclosing a probe for phage-display containing progesterone (*i.e.*, "drug") cross-linked to BSA, Pecht et al and the disclosure in the present specification at page 3, lines 19-22 are cited to show that the claimed cross-linkers (*e.g.*, glutaraldehyde) are commonly used to cross-link "drugs" to BSA. Odink et al is allegedly cited as disclosing methods for producing human polypeptides using methods of recombinant DNA technology. Barbas et al is cited as disclosing the use of nitrocellulose filters with isopropyl-b-D-thiogalactopyranoside to capture a phage from plated phage culture. However, even if the skilled artisan were to combine the disclosures of the Gram et al, Odink et al, Pecht et al, the Examiner's interpretation of the specification at page 3, lines 19-22, and Barbas et al the combined disclosures still fail to compensate for the aforementioned deficiencies in the disclosure of Gram et al (no disclosure of human cDNA) and the combined disclosures of Gram et al and Pecht et al (nonanalogous art), or the combined disclosures of Gram et al, Odink et al, and Pecht et al.

Accordingly, Applicants request withdrawal of these grounds of rejection.

Finally, Applicants remind the Examiner that withdrawn subject matter, including Claim 14, should be rejoined and examined once the elected subject matter has been found allowable. Acknowledgement to this effect is requested.

Applicants submit that the present application is now in condition for allowance.

Early notification of such action is earnestly solicited.

Respectfully submitted,

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